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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/574,297	CASTADO ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,23-29,31,32,34,35,53-66,69,70 and 72* is/are pending in the application.

4a) Of the above claim(s) *1-10, 12-13, 23-28, 31, 34-35, 55-64, 69-70, and 72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,29,32,53,54,65 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicants amendment and response filed 10-7-09. Claims 1-13, 23-29, 31-32, 34-35, 53-66, 69-70, and 72 pending. Claims 11, 29, 32, 53-54, and 65-66 are under examination. Claims 11, 29, and 32 are amended. Claims 30, 33, 36, 67-68 and 71 have been cancelled. Claims 1-10, 12-13, 23-28, 31, 34-35, 55-64, 69-70, and 72 is withdrawn.

Rejections Withdrawn

2. In view of the Applicant's amendments and remarks the following rejections are withdrawn.

a) Rejection to claims 11, 29-30, 32-33 36, and 53-54 under 35 U.S.C. 103(a) as being unpatentable over Novotny et al (US Patent No. 7,479,283 Date January 20, 2009 Date Filed May 25, 1995) and Oliver et al (Vaccine Vol. 20, 2002 pgs. 235-241) as evidenced by Kinnear et al (Infection and Immunity Vol. 69 No. 4, 2001 pgs. 1983-1993) is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 112, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejection of claims 65-66 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for the reasons set forth in the previous office action. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant arguments:

Applicants arguments filed in response to the 35 U.S.C. 112, first paragraph on October 7, 2009 is carefully considered, but not found to be persuasive for the reasons below.

Applicants are not claiming compositions made from new or unknown biological materials and the currently pending claims recite immunogenic compositions comprising a known polypeptide, namely BrkA (SEQ ID NO:34). Applicants state at the time of filing, the BrkA polypeptide had already been described in the scientific literature; much was known about its structure, including its sequence and structural regions. See Oliver et al. (2002) Vaccine, 20:235-41 (stating in the abstract that "BrkA is synthesized as a 103 kDa precursor that is processed in to a surface-associated N-terminal 73 kDa passenger domain, and an outer-membrane embedded C-terminal 30 kDa transporter moiety"). Applicants state the specification provides guidance regarding the epitopes of SEQ ID NO: 34 on page 99, Table 5 (predicted B-cell epitopes) and Table 6 (predicted T-cell epitopes). These predicted epitopes are identified by position within SEQ ID NO: 34 and further guidance regarding the length and structure of fragments comprising the predicted epitopes. Applicants draw the examiner's attention to the new set of Written Description Training Materials published in 2008 which "supersede and replace the 1999 training materials," particularly Example 11.

Examiners response to Applicant arguments:

In response to applicant's statement in as set forth supra, the specification discloses SEQ ID NO:34 which corresponds to a *Bordetella* autotransporter BrkA protein of *Bordetella pertussis* (see pg. 33) and the specification provides guidance for an amino acid sequence that has 85% identity to SEQ ID NO:34 which meets the written description provision of 35 USC 112, first paragraph in view of the Written Description Training Materials published in 2008 which "supersede and replace the 1999 training materials," particularly Example 11. However the claims are directed to vaccine compositions comprising an immunogenic composition comprising a polypeptide comprising an amino acid sequence sharing at least 85% identity with SEQ ID NO: 34 or an antigenic fragment of at least 15 contiguous amino acids of SEQ ID NO: 34 capable of stimulating a protective immune response in an animal *to Bordetella spp.* wherein said vaccine compositions are drawn to a broad genus polypeptides that are at least 85% identical to SEQ ID NO: 34. Moreover, the specification does not teach the protective immunoepitope(s) of a SEQ ID NO: 34 so that one of skill in the art can envision which regions of the amino acid can be conservatively substituted and still retain immunogenicity and protectiveness. Further, the specification does not teach which 5% or 4% or 3% or 2% or 1% of SEQ ID NO: 34 can be

changed and still retain the ability to protect against infection. The claims are drawn to a large number of variants having different possibilities of changes to the amino acid sequence of SEQ ID NO: 34. The specification does not teach an example of any variant of SEQ ID NO: 34 of the instant protein that protects from infection.

Even though one could screen for which changes in SEQ ID NO: 34 will maintain protection from infection, the courts have held that possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. The disclosure of compositions comprising a known polypeptide, namely BrkA (SEQ ID NO: 34), is insufficient to describing the large and variant genus of proteins and the scope of which is set forth above. Therefore, the specification fails to describe at least a substantial number of members of the claimed genus of immunogenic compositions capable of stimulating a protective immune response in an animal *to* a given *Bordetella* species.

As outlined previously, the instant claims are drawn to vaccine compositions capable of stimulating a protective immune response in an animal *to Bordetella spp.* wherein said vaccine compositions are drawn to broad genus polypeptides that are at least 85% identical to SEQ ID NO: 34.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of *vaccine* compositions comprising a polypeptide that is at least 85% identical, Applicant must adequately describe the antigenic determinants (immunoepitopes) that elicit a protective immune response directed against a given *Bordetella* species not just those determinants that would elicit an immune response to the polypeptide itself since given polypeptide can be immunogenic but not induce an protective immune response directed against a given *Bordetella* species.

The specification, however, does not disclose distinguishing and identifying features of a representative number of members of the genus of immunogenic compositions to which the

claims are drawn, such as a correlation between the structure of the immunoepitope and its recited function (to elicit a protective immune response directed against a given *Bordetella* species), so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of immunogenic compositions. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the immunoepitope or which amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of immunoepitopes to which the claims are based; the specification fails to adequately describe at least a substantial number of members of the claimed genus of immunogenic compositions capable of stimulating a protective immune response in an animal *to* a given *Bordetella* species.

The dictionary definition of vaccine is "A prophylactic or therapeutic material containing antigens derived from one or more pathogenic organisms which, on administration to man or animal, will stimulate active immunity and protect against infection with these or related organism (i.e. produce protective immunity)." (The Dictionary of Immunology, Herbert et al eds, Academic Press, 1995).

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical*

Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Greenspan et al. (*Nature Biotechnology* **7**: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. Therefore,

absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of immunoepitopes, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of vaccine compositions capable of stimulating an immune response in an animal *to* a given *Bordetella* species (as opposed to the polypeptide) said composition comprising a polypeptide that is at least 85% identical to SEQ ID NO: 34. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of immunoepitopes (antigenic determinants) is not deemed representative of the genus of vaccine compositions to which the claims refer and therefore the claimed invention is not properly disclosed.

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Enablement

4. The rejection of claims 65-66 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for the reasons set forth in the previous office action. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant arguments:

Applicants arguments filed in response to the 35 U.S.C. 112, first paragraph on October 7, 2009 is carefully considered, but not found to be persuasive for the reasons below.

Applicants state claim 11, from which the rejected claims depend, has been amended to recite a composition comprising PT, FHA, and a polypeptide having 85% identity with SEQ ID NO:34 (BrkA). Applicants state Example 13 also discloses that the protection conferred by DTPa-2 BrkA against B. pertussis strain 18323 was statistically equivalent to that provided by the Depew (whole cell B. pertussis) and DTPa-3 (PT, FHA, and pertactin) vaccination. Applicants state the references cited in the rejection fail to establish that practicing the claims as amended would require undue experimentation.

Examiners response to Applicant arguments:

In response to applicant's statement as set forth supra, in regards to Applicants amendment of claims and Applicants response disclosing Example 13 is unpersuasive for the reasons set forth supra. To begin with the claims are to any vaccine comprising an immunogenic composition comprising: a polypeptide comprising: a) an amino acid sequence sharing at least 85% identity with SEQ ID NO:34 or antigenic fragment of at least 15 contiguous amino acids of SEQ ID NO:34; b) a *Bordetella* adhesin of FHA; c) a pertussis toxin; and d) at least one different *Bordetella* antigen selected from the group consisting of : C) at least one *Bordetella* adhesin selected from the group consisting of fimbriae 2 and/or 3 or pertactin; and D) at least one *Bordetella* toxin/invasin or antigens involved in toxin/invasin secretion selected from the group consisting of adenylate cyclase, dermonecrotic toxin (Dnt), Type III ss or lipopolysaccharide as claimed encompassing all vaccines to an unnamed pathogen, comprising immunogenic composition which encompasses at exactly four different *Bordetella* antigens. Moreover, the instant claims encompass fragments of the recited proteins as well as proteins with at least 85% identity to SEQ ID NO: 34.

Moreover, the specification does not teach the protective immunoepitope(s) of a SEQ ID NO: 34 so that one of skill in the art can envision which regions of the amino acid can be conservatively substituted and still retain immunogenicity and protectiveness. Further, the specification does not teach which 5% or 4% or 3% or 2% or 1% of SEQ ID NO: 34 can be changed and still retain the ability to protect against infection. The claims are drawn to a large number of variants having different possibilities of changes to the amino acid sequence of SEQ ID NO: 34. The specification does not teach an example of any variant of SEQ ID NO: 34 of the instant protein that protects from infection. Therefore, the specification is silent with regards to what specific immunoepitopes must be present in each antigen to elicit a protective immune response. Moreover, the specification is only limited to an immunogenic composition aforementioned above that reduces infection. Although the specification does disclose *in vivo* methods of determining the immune response in mice challenges. The challenged data as set forth supra does not demonstrate that the vaccine (unnamed to a pathogen) composition confers "protection" against any type of infection. The specification does not disclose any working example including Example 13 aforementioned above in Applicants response that any vaccine,

comprising an immunogenic composition as set forth supra will work against a given infection. Therefore the rejection is maintained.

As outlined previously, the specification is not enabled for any vaccine to an unnamed pathogen comprising an immunogenic composition comprising: a polypeptide comprising: a) an amino acid sequence sharing at least 85% identity with SEQ ID NO:34 or antigenic fragment of at least 15 contiguous amino acids of SEQ ID NO:34; b) a *Bordetella* adhesin of FHA; c) a pertussis toxin; and d) at least one different *Bordetella* antigen selected from the group consisting of : C) at least one *Bordetella* adhesin selected from the group consisting of fimbriae 2 and/or 3 or pertactin; and D) at least one *Bordetella* toxin/invasin or antigens involved in toxin/invasin secretion selected from the group consisting of adenylate cyclase, dermonecrotic toxin (Dnt), Type III ss or lipopolysaccharide as claimed.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

(A) The nature of the invention;

(B) The breadth of the claims;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention: The instant claims are drawn to any vaccine to an unnamed pathogen comprising an immunogenic composition comprising: a polypeptide comprising: a) an amino acid sequence sharing at least 85% identity with SEQ ID NO: 34 or antigenic fragment of at least 15 contiguous amino acids of SEQ ID NO: 34;

b) A *Bordetella* adhesin of FHA;

c) A pertussis toxin; and

d) at least one different *Bordetella* antigen selected from the group consisting of: C) at least one *Bordetella* adhesin selected from the group consisting of fimbriae 2 and/or 3 or pertactin; and D) at least one *Bordetella* toxin/invasin or antigens involved in toxin/invasin secretion selected from the group consisting of adenylate cyclase, dermonecrotic toxin (Dnt), Type III ss or lipopolysaccharide.

Breadth of the claims: The claims encompass all vaccines to an unnamed pathogen, comprising an immunologically effective amount of an immunogenic composition which encompasses at exactly four different *Bordetella* antigens wherein the antigens are: a polypeptide comprising: a) an amino acid sequence sharing at least 85% identity with SEQ ID NO: 34 or antigenic fragment of at least 15 contiguous amino acids of SEQ ID NO: 34;

b) A *Bordetella* adhesin of FHA;

c) A pertussis toxin; and

d) at least one different *Bordetella* antigen selected from the group consisting of: C) at least one *Bordetella* adhesin selected from the group consisting of fimbriae 2 and/or 3 or pertactin; and D) at least one *Bordetella* toxin/invasin or antigens involved in toxin/invasin secretion selected from the group consisting of adenylate cyclase, dermonecrotic toxin (Dnt), Type III ss or lipopolysaccharide.

Guidance of the specification/The existence of working examples: The specification discloses pre-immunization with different formulations comprising combinations of pertussis toxin (PT), and FHA, BrkA, etc. (see 100). The specification discloses mice vaccinated with a challenge infection of *Bordetalla pertussis* strain Tohama, *Bordetalla pertussis* strain 18323, *and Bordetalla pertussis* strain parapertussis after pre-immunization (see pgs. 101-103 and Figure 1). The specification discloses five mice in each group were killed at 4 different times (2 hours, 2, 5 and 8 days) after challenge and the lungs were removed aseptically and homogenized individually and the CFU/lung was determined by counting the colonies (see pg. 102). The specification discloses in contrast, the addition of BrkA to a DTPa-2 formulation reduces infection, and in combination with pertussis toxin (PT) and FHA, BrkA can produce additional reduction in infection. Furthermore the DTPa-3 BrkA vaccine provided reduction of infection

from challenge after 2 and 5 days but less reduction of infection after day 8 (see Example 12) (see pg. 103 and Figure 1). The challenged data as set forth supra does not demonstrate that the vaccine (unnamed to a pathogen) composition confers "protection" against any type of infection. It merely shows that said composition reduces infection. Although the specification does disclose *in vivo* methods of determining the immune response in mice challenges, the specification does not disclose any working example that any vaccine, comprising an immunogenic composition as set forth supra will work against a given infection. A vaccine by definition must provide protection against an infection demonstrable by challenge experiments. The specification is devoid of any teaching that the claimed vaccine discloses a protective response against any subject. Moreover, the instant claims encompass fragments of the recited proteins as well as proteins with at least 85% identity to SEQ ID NO: 34. However, the specification is silent with regard to what specific immunoepitopes must be present in each antigen to elicit a protective immune response.

State of the art: Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection (Chandrashekar et al., US Patent 6,248,329, col. 1, lines 35-41). It is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity. Ellis (Chapter 29 of Vaccines, Plotkin, et al. (eds) WB Saunders, Philadelphia, 1998, especially p. 571, paragraph 2) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.., and thus protect the host against attack by the pathogen." Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further

teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). For the reasons set forth supra, the state of the art is has limitations to a vaccine composition and the state of the art is unpredictable with regard any vaccine composition comprising a conjugate.

In conclusion, the claimed invention is not enabled for any vaccine to an unnamed pathogen comprising an immunogenic composition comprising: a polypeptide comprising: a) an amino acid sequence sharing at least 85% identity with SEQ ID NO:34 or antigenic fragment of at least 15 contiguous amino acids of SEQ ID NO:34; b) a *Bordetella* adhesin of FHA; c) a pertussis toxin; and d) at least one different *Bordetella* antigen selected from the group consisting of : C) at least one *Bordetella* adhesin selected from the group consisting of fimbriae 2 and/or 3 or pertactin; and D) at least one *Bordetella* toxin/invasin or antigens involved in toxin/invasin secretion selected from the group consisting of adenylate cyclase, dermonecrotic toxin (Dnt), Type III ss or lipopolysaccharide. The claims encompass all vaccines, comprising an immunogenic composition as set forth supra without disclosing what the vaccine will treat or prevent. The specification fails to teach that the immunogenic composition as set forth can produce a protective response in the host, as is requisite of a vaccine composition. The state of the art teaches that there are limitations to a vaccine composition and the state of the art is unpredictable. In view of the lack of support in the art and specification for an effective vaccine, it would require undue experimentation on the part of the skilled artisan to make and use the vaccine as claimed; therefore the claims are not enabled. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed composition.

New Grounds of Rejection

Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 11, 29, 32, and 53-54 rejected under 35 U.S.C. 103(a) as being unpatentable over Novotny et al (US Patent No. 7,479,283 Date January 20, 2009 Date Filed May 25, 1995), Oliver et al (Vaccine Vol. 20, 2002 pgs. 235-241), and Peetermans et al (WO/1997/000697 Publication Date September 1, 1997) as evidenced by Kinnear et al (Infection and Immunity Vol. 69 No. 4, 2001 pgs. 1983-1993) and as evidenced by Pagliaccia et al (Arch Microbiol 168 pgs. 437-440 1997).

The instant claims are drawn to an immunogenic composition comprising exactly four different *Bordetella* antigens wherein the antigens are a polypeptide comprising: a) an amino acid sequence sharing at least 85% identity with SEQ ID NO:34 or antigenic fragment of at least 15 contiguous amino acids of SEQ ID NO:34; b) a *Bordetella* adhesin of FHA; c) a pertussis toxin; and d) at least one different *Bordetella* antigen selected from the group consisting of : C) at least one *Bordetella* adhesin selected from the group consisting of fimbriae 2 and/or 3 or pertactin; and D) at least one *Bordetella* toxin/invasin or antigens involved in toxin/invasin secretion selected from the group consisting of adenylate cyclase, dermonecrotic toxin (Dnt), Type III ss or lipopolysaccharide.

Novotny et al teach an acellular pertussis vaccine comprising a combination of *Bordetella pertussis* antigens, wherein said combination consist of isolated and purified 69 kDa antigen of *Bordetella pertussis* and isolated and purified filamentous haemagglutinin (FHA) antigen of

Bordetella pertussis, wherein the 69 kDa antigen (pertussis toxin) and the filamentous haemagglutinin antigen are present in a ratio of from 1:1 to 1:10, wherein the vaccine is effective in inducing protection in a mammal to subsequent challenge by a virulent strain of *Bordetella pertussis* (see claim 1). Furthermore the antigens of Novotny et al teach an immunogenic composition comprising 69 kDa antigen (pertussis toxin) that is expressed during Bvg+late phase of Bordetella infection and comprising a polypeptide (FHA) that is expressed during Bvg+early phase of Bordetella infection (see pgs. 16-17 Figure 2) (see pg. 1983 and column 2) as evidenced by Kinnear et al.

Novotny et al differs from the instant invention in that they don't explicitly disclose the BrkA protein (SEQ ID NO: 34) in their vaccine composition. Furthermore, Novotny et al does not teach an immunogenic composition comprising at least one different *Bordetella* antigen selected from the group consisting of C) at least one *Bordetella* adhesin selected from the group consisting of fimbriae 2 and/or 3 or pertactin; and D) at least one *Bordetella* toxin/invasin or antigens involved in toxin/invasin secretion selected from the group consisting of adenylate cyclase, dermonecrotic toxin (Dnt), Type III ss or lipopolysaccharide.

Oliver et al teach polyclonal antibodies were raised to BrkA protein by using 1mg antigen per rabbit and 4 immunizations (see abstract pg. 236 column1 Section 2.3) which correlate to an immunogenic composition comprising a) an amino acid sequence sharing at least 85% identity with SEQ ID NO: 34 or an antigenic fragment, because the sequence of a polypeptide is an inherent feature of a polypeptide specified below. The specification disclose SEQ ID NO: 34 known as BrkA protein (see pg. 33 Auto transporter proteins)). It is deemed, in absence of evidence to the contrary that the BrkA protein of Oliver et al. is the same as an amino acid sequence at least 80% identical to SEQ ID NO: 34 of the instant invention. Therefore given the polypeptide of the instant invention and the BrkA protein of Oliver et al. are deemed to be the same and the sequence of a polypeptide is an inherent feature of a polypeptide thus both polypeptides would necessarily have the same amino acid sequence. Moreover, Oliver et al teach anti-BrkA antibodies were shown to boost the existing bactericidal mechanisms. Oliver et al teach the addition of anti-BrkA antiserum to human serum neutralizes complement resistance, thus indicating the possibility of preventing infection or colonization against Bordetella pertussis (see pg. 235 column last paragraph and pg. 240 column 1).

Peetermans et al teach a multivalent vaccine for the amelioration or treatment of more than one disease. Peetermans et al teach formulations comprising at least one other component selected from antigens which afford protection against one or more of the following: Hepatitis A virus (HAV), diphtheria, tetanus, pertussis, Hepatitis B and polio. Peetermans et al teach acellular pertussis diphtheria-tetanus pertussis vaccine (DTPa) combination vaccine comprising a whole cell or an accellular pertussis component which typically consists of two or three antigens (i.e. detoxified PT, FHA or 69kDa) (see pg. 1 lines 25-30), wherein 69kDa is pertactin as evidenced by Pagliaccia et al (see pg. 437). Peetermans et al teach it would be desirable to add other antigens to a combination vaccine for the prevention of diseases (see pg. 2 lines 1-5).

According to MPEP 2144.06, "It is prima facie obvious to combine each immunogenic composition of which is taught by the prior art to be useful for the same purpose, in order to form a immunogenic combination of antigens to be used for the very same purpose ....[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Therefore, it would have been obvious to use SEQ ID NO: 34, FHA, pertussis toxin, and pertactin because these antigens are taught to be useful for that purpose.

Conclusion

6. No claims are allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert B Mondesi/
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